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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Gerardo Castillo et al.                      Art Unit : 1614  
Serial No. : 10/762,444                                      Examiner : Unknown  
Filed : January 21, 2004  
Title : POLYHYDROXYLATED AROMATIC COMPOUNDS FOR THE  
TREATMENT OF AMYLODOSIS AND ALPHA-SYNUCLEIN FIBRIL  
DISEASES

**Mail Stop Amendment**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**TRANSMITTAL LETTER**

Dear Sir:

Transmitted herewith are an Information Disclosure Statement and Forms PTO-1449 (3) pages and cited references for filing in connection with the above-identified application. Because this Information Disclosure Statement is filed prior to receipt of a first office action on the merits in the above-referenced application, no fee is due. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 06-1050, as stated below:

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 06-1050. A duplicate of this sheet is enclosed.

Respectfully submitted,

Dale L. Rieger  
Reg. No. 43,045

Attorney Docket No. 17170-002002  
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**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**  
**IN ACCORDANCE WITH 37 C.F.R. 1.97-1.98**

Dear Sir:

Because this Information Disclosure Statement is filed before the receipt of a First Office Action on the Merits for the above-captioned application, a filing fee is not enclosed. If a fee is due, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 06-1050.

In accordance with the duty of disclosure imposed by 37 C.F.R. §1.56 to inform the Patent Office of all references known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Supplemental Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§1.97-1.98. Forms PTO-1449 (3 pages) and hard copies of the references are provided herewith in connection with the above-captioned application.

The documents cited on the Forms PTO-1449 are in the English language. Hence, in accordance with the requirements of 37 C.F.R. 1.98, as amended effective March 16, 1992, no further explanation of the listed items is necessary.

Applicant also makes known to the Examiner the following pending U.S. applications that have one or more common inventors and/or are commonly owned:

<b>U.S.S.N.(App. no.)</b>	<b>Filing Date</b>	<b>Docket No.</b>
10/077,596	02/15, 2002	17170-006001

Applicant : Gerardo Castillo et al.  
Serial No. : 10/762,444  
Filed : January 21, 2004  
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Although these documents are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the references, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. 1.97(h), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. 1.56(b) exists.

Applicant respectfully requests that the Examiner review the foregoing references and they be made of record in the file history of the above-captioned application.

Respectfully submitted,

Date: 8/20/04

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Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 17170-002002	Application No. 10/762,444
<b>Information Disclosure Statement by Applicant</b> (Use several sheets if necessary) (37 CFR §1.98(b))		Applicant Gerardo Castillo et al.	
		Filing Date January 21, 2004	Group Art Unit 1614

### U.S. Patent Documents

Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate

### Foreign Patent Documents or Published Foreign Patent Applications

Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation	
							Yes	No
	A	00/57707	10/05/00	PCT				
	B	02/062422	08/15/02	PCT				
	C	02/076381	10/03/02	PCT				
	D	99/09999	03/04/99	PCT				

### Other Documents (include Author, Title, Date, and Place of Publication)

Examiner Initial	Desig. ID	Document
	E	"Progress Report on Alzheimers Disease," The National Institute on Aging, National Institutes of Health, 1997.
	F	Baumann et al, "A simple isolation method for the major catechins in green tea using high-speed countercurrent chromatography," <i>J. Natural Prod.</i> 64:353-355, (2001)
	G	Braquet et al. "Ethnopharmacology and the Development of Natural PAF Antagonists as Therapeutic Agents," <i>Journal of Ethnopharmacology</i> , 32:135-139, (1991)
	H	Calis et al, "Flavonoid, Iridoid, and Lignan Glycosides from <i>Putoria calabrica</i> ," <i>J. Nat. Prod.</i> 64:961-964, (2001)
	I	Clark et al, "Islet Amyloid, Increased A-Cells, Reduced B-Cells and Exocrine Fibrosis: Quantitative Changes in The Pancreas in Type 2 Diabetes," <i>Diabetes Res.</i> 9:151-159, (1988)
	J	Czochanska et al, "Direct Proof of a Homogeneous Polyflavan-3-ol Structure for Polymeric Proanthocyanidins," <i>J.C. S. Chem. Comm.</i> pp. 375-377, (1979)
	K	Derwent World Patents Index, Dialog File Number 351 Accession Number 12134240; JP 10245342A "Agent for Reducing Nerve Cell Toxicity of Beta-Amyloid Protein - Contains Tea Polyphenol"
	L	Ferreira et al, "Tetrahedron Report Number 308: Diversity of Structure and Function in Oligomeric Flavanoid," <i>Tetrahedron</i> 48:1743-1803, (1992)
	M	Fletcher et al, "Plant Proanthocyanidins. Part 3. Conformational and Configurational Studies of Natural Procyanidins," <i>JCS Perkin</i> 1:1628-1637, (1977)
	N	Gujer et al, "Glucosylated Flavonoids and Other Phenolic Compounds From Sorghum," <i>Phytochemistry</i> 25:1431-1436 (1986)
	O	Hashimoto et al, "Tannins and related Compounds. XC. 8-C-Ascorbyl (-)-Epigallocatechin 3-)-Gallate and novel dimeric Flavan-3-ols, Oolonghomobisflavans A and B from Oolong tea," <i>Chem Pharm. Bull.</i> 37(12) 3255-3263 (1989)
	P	Hemingway et al, "Linkage Isomerism in Trimeric and Polymeric 2,3-cis-Procyanidins," <i>J. Chem. Soc. Perkins Trans.</i> 1:1209-1216 (1982)
	Q	Ho et al. "Phytochemicals in Teas and Rosemary and Their Cancer-Preventive Properties," <i>ACS Symp. Ser. (Food Phytochemicals for Cancer Prevention II)</i> vol. 547, pp. 2-19 1994.

Examiner Signature

Date Considered

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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**Other Documents (include Author, Title, Date, and Place of Publication)**

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	R	Hsiao et al. "Age-related CNS Disorder and early death in transgenic FVB/N mice overexpressing alzheimer amyloid precursor proteins." <i>Neuron</i> , vol. 15, 1203-1218, Nov., 1995.
	AB	Ishimaru et al, "Flavan-2-ol and Procyanidin Glycosides from <i>Quercus Miyagii</i> ," <i>Phytochemistry</i> 26:1167-1170, (1987)
	AC	Jain et al. "Antiinflammatory Effects of an Ayurvedic Preparation, Brahmi Rasayan, in Rodents," <i>Indian Journal of Experimental Biology</i> , 32:633-636 (1994)
	AD	Jones et al, "The Condensed Tannins of Pasture Legume Species," <i>Photochemistry</i> , 15:1407-1409 (1976)
	AE	Kashiwada et al, "Tannins and Related Compounds. XCIII. <sup>1)</sup> Occurrence of Enantiomeric Proanthocyanidins in the Leguminosae Plants, <i>Cassia fistula</i> L. and <i>C.javanica</i> L.," <i>Chem. Pharm. Bull.</i> 38:888-893 (1990)
	AF	Kim et al, "Neuroprotective Constituents from <i>Hedyotis diffusa</i> ," <i>J. Nat. Prods.</i> 64:75-78, (2001)
	AG	Latimer et al. "71. Inhibitors of Amyloid- $\beta$ Aggregation: Dimeric Catechols Inhibit Aggregation and Deposition of A $\beta$ ," American Chemical Society 221 <sup>st</sup> National Meeting, San Diego, CA April 1-5, 2001 (MEDI 071) [posted on 03/23/01]
	AH	Levine. "Thioflavine T interacton with amyloid B-sheet structures." <i>Amyloid: Int. J. Exp. Clin. Invest.</i> 2:1-6, (1995)
	AI	Lorenzo et al, "Pancreatic islet cell toxicity of amylin associated with type-2 diabetes mellitus," <i>Nature</i> 368:756-760, (1994)
	AJ	Mathews et al, "Method for estimation of Proanthocyanidins based on their acid depolymerization in the presence of nucleophiles," <i>J. Agric. Food Chem.</i> 45:1195-1201, (1997)
	AK	Mattice et al, "Molecular weight averages and <sup>13</sup> C NMR intensities provide evidence for branching in proanthocyanidin polymers," <i>Phytochem.</i> 23(6):1309-1311, (1984)
	AL	Morimoto et al, "Tannins and Related Compounds. LXI. <sup>1)</sup> Isolation and Structure of Novel Bi- and Triflavanoids from the leaves of <i>Cassia fistula</i> L.," <i>Chem. Pharma. Bull.</i> 36:39-47, (1988)
	AM	Nonaka et al, "Tannins and Related Compound. XV. <sup>1)</sup> A New Class of Dimeric Flavan-3-ol Gallates, Theasinensins A and B, and Proanthocyanidin Gallates from Green Tea Leaf. (1)," <i>Chem. Pharm. Bull.</i> 31:3906-3914, (1983)
	AN	Patent Abstracts of Japan citing Japanese Patent 10-245342 published September 14, 1998, "Agent for reducing neural toxicity of beta-amyloid protein"
	AO	Porter et al, "Isolation of three naturally occurring O- $\beta$ -glucopyranosides of procyanidin polymers," <i>Phytochemistry</i> 24:567-569, (1985)
	AP	Porter, L.J, "Flavans and proanthocyanidins," Chapter 2 in <i>Flavans and proanthocyanidins--Advances in Research since 1986</i> , J B Harborne (Ed.) London: Chapman and Hall pp. 23-55, 1994
	AQ	Porter, J.J, "Flavans and proanthocyanidins," Chapter 2 in <i>The Flavanoids--Advances in Research since 1980</i> , J B Harborne (Ed.), London: Chapman and Hall, pp. 21-62, 1988
	AR	Prieur et al, "Oligomeric and polymeric procyanidins from grape seeds," <i>Phytochem.</i> 36:781-784, 1994
	AS	Sang et al, "Iridoid Glycosides from the leaves of <i>Morinda citrifolia</i> ," <i>J. Nat. Prod.</i> 64:799-800 (2001)
	AT	Santos-Buelga, C. and A. Scalbert, "Proanthocyanidins and tannin-like compounds - nature, occurrence, dietary intake and effects on nutrition and health," <i>J. Sci.. Food Agri.</i> 80: 1094-1117, (2000)

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	AU	Snow. "Proteoplycans in the pathogenesis of alzheimer's disease and other amyloidoses." <i>Neurobiology of Aging</i> , 10:481-497, (1989)
	AV	Stappenbeck et al., "80. Inhibitors of Amyloid- $\beta$ Aggregation: Histidine Residues in A $\beta$ Play a Crucial Role in Aggregation," American Chemical Society 221 <sup>st</sup> National Meeting, San Diego, CA April 1-5, 2001 (MEDI 080) [posted on 03/23/01]
	AW	Steinberg. "Uncaria Tomentosa (cat's Claw) A wondrous herb from the peruvian rain forest." <i>Townsend Letter for Doctors</i> -pp, 442-443, may 1994.
	AX	Sugita-Konishi et al., "Epigallocatechin gallate and gallic acid in green tea catechins inhibit extracellular release of Vero toxin from enterohemorrhagic <i>Escherichia coli</i> O157:H7," <i>Biochimica et Biophysica Acta</i> 1472:42-50 (1999)
	AY	Tamaoka et al. "Amyloid B protein 1-42/43(AB 1-42/43) in crebellar diffuse plaques: enzyme-linked immunosorbent assay and immunocytochemical study." <i>Brain Research</i> 67:151-156 (1995)
	AZ	Tamaoka et al. "Biochemical evidence for the long tail form of amyloid B protein as a seed molecule in cerebral deposits of alzheimer's disease." <i>Biochemical and biophysical research communications</i> , 205(1): 834-842, (1994)
	BA	Thompson et al., "Plant Proanthocyanidins. Part 1. Introduction; the Isolation, Structure, and Distribution in Nature of Plant Procyranidins," <i>J. Chem. Soc. Perkins Trans.</i> 1: 1387-1399 (1972)
	BB	Tückmantel, "Studies in Polyphenol Chemistry and Bioactivity. 1. Preparation of Building Blocks from (+)-Catechin. Procyranidin Formation. Synthesis of the Cancer Cell Growth Inhibitor, 3-O-Galloyl-(2R,3R)-epicatechin-4 $\beta$ ,8-[3-O-Galloyl-(2R,3R)-epicatechin]," <i>J. Am. Chem. Soc.</i> 121:12073-12081 (1999)
	BC	Wirth et al. "Pharmacologically active procyanidines from the bark of Uncaria tomentosa." <i>Phytomedicine</i> , vol. 4 (3), pp. 265-266, 1997.
	BD	Zhang et al., "Potentillanin, A Biflavanoid and a procyanidin glycoside from potentilla viscosa," <i>Phytochemistry</i> 27:3277-3280, (1988)

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